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# COST EVALUATION OF COLLAGENASE *CLOSTRIDIUM HISTOLYTICUM* VERSUS SURGERY FOR DUPUYTREN'S CONTRACTURE

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## ABSTRACT

**OBJECTIVE** To evaluate whether collagenase injections would be a cost-effective alternative to surgery for Dupuytren's contracture in Malta.

**METHOD** An average of fifty patients per year requires surgery to correct Dupuytren's contracture in Malta. The price of collagenase injections was obtained from published pharmacoeconomic studies in Spain, United Kingdom and United States. The cost to treat multiple affected joints using collagenase injections at the different prices was compared to the costs associated with surgery in both the government and private hospital setting. A proposed price at which collagenase injections would be more cost-effective than surgery to treat two affected joints in Malta was calculated.

**KEY FINDINGS** The cost of surgery in the private hospital setting is significantly higher than that in the government hospital setting. The price of collagenase in the United States is significantly higher than in Europe. At the prices available in Europe, collagenase use in Malta would not confer significantly increased costs when treating one, two or three affected joints, both in the government and private hospital setting. Treating two affected joints rather than one affected joint does not significantly increase costs, however treating three affected joints significantly increases costs, in both hospital settings. For collagenase injections to be cost-effective in Malta, they would need to be priced at 77 Euro per vial or less.

**CONCLUSION** If all patients were to be administered the injection instead of undergoing surgery, the hospital would be able to accommodate 20 additional total knee replacements each year. With surgery costs in Malta being much less than in other European countries, there could be a possibility for Malta to attract patients from other countries. Collagenase injections would offer a less invasive treatment for the patients, and if priced at 77 Euro per vial or less, would provide a more cost-effective option to the government hospital.

**KEYWORDS** Dupuytren's contracture, collagenase, *Clostridium histolyticum*, open fasciectomy, costs

## INTRODUCTION

Dupuytren's Contracture (DC) is defined as a thickening of the fibrous tissue layer underneath the skin of the palm and fingers.<sup>1</sup> The condition is not usually painful; however over time, the collagen thickening causes contracture, leading to the affected fingers becoming permanently flexed. A diagnosis of DC is usually made when there is a positive Hueston tabletop test, where the patient is unable to fully extend the fingers and place them flat on a surface.<sup>2</sup>

The first signs of Dupuytren's Contracture are the formation of palpable collagen nodules in the palm of the hands. These collagen deposits tend to form collagen cords which usually extend longitudinally. Over time, the collagen thickens and shortens, causing the affected fingers to flex inwardly at the metacarpophalangeal joints or at the proximal interphalangeal joints. This contracture is usually irreversible.<sup>3,4</sup>

Various treatment options are available<sup>5</sup>; the most commonly used option is surgery, including partial or open fasciectomy.<sup>6,7</sup> In 2010, the Food and Drug Administration (FDA) followed by the European Medicines Agency in 2011, approved the first pharmacological treatment to correct Dupuytren's Contracture; an injection containing the enzyme collagenase *Clostridium histolyticum* (CCH). Collagenase injections are administered when there is a palpable cord, with a maximum of three injections given per cord at monthly intervals. Studies carried out concluded that CCH injections were a safe and effective alternative to surgery.<sup>3,8,9</sup>

It was estimated that in 2011 in England, DC related costs amounted to £41,576,141.<sup>10</sup> Economic studies were carried out in the United Kingdom (UK)<sup>11</sup>, Spain<sup>12</sup> and the United States (US).<sup>13</sup> Studies undertaken in UK and Spain concluded that CCH injections, quoting the retail price of CCH injections at the time of the study, would reduce costs associated with treatment of DC.<sup>11,12</sup> The study carried out in the US concluded that for CCH injections to be cost-effective, the price had to be one tenth of the retail price at the time of the study.<sup>13</sup>

The study carried out in Malta aimed to assess the cost-effectiveness of CCH injections at the various prices available in other countries to the cost of open fasciectomy, both in the government and private hospital settings.



## METHOD

Determination of the most common procedure to correct DC used in Malta was undertaken through discussions with all orthopaedic surgeons. Open fasciectomy was costed both in the government hospital and private hospital setting. Costs included the salary of all the healthcare professionals, cost of drugs used, utility costs and equipment costs.

The prices of CCH injections were obtained from economic studies published in the UK, Spain and the US, and converted to Euro where necessary. The cost of treating multiple affected joints was calculated for each of the prices quoted and compared to surgery in both hospital settings. An assessment was undertaken to evaluate whether the introduction of CCH injections would be more cost-effective for the different settings when compared to surgery. A proposed price for CCH injections to be cost-effective in the Maltese healthcare system was calculated.

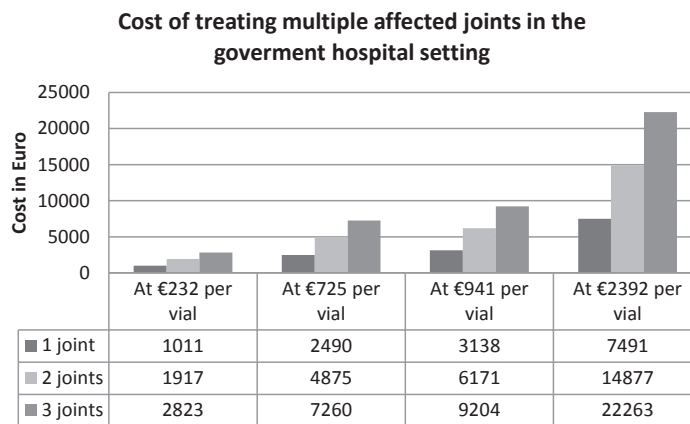
## RESULTS

Open fasciectomy at the government hospital costs €987 if performed under local anaesthesia and €1,196 if performed under general anaesthesia, including pre-operative tests,

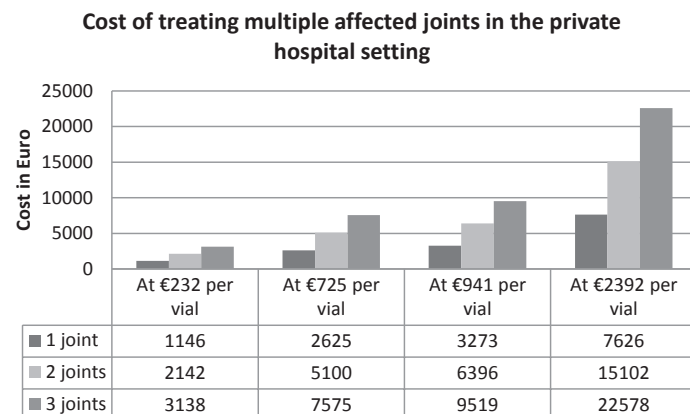
orthopaedic out-patient assessments and post-operative hand therapy sessions. The cost of surgery in a private hospital setting, including all the pre- and post-operative care is of €3,361. The cost of surgery in the private hospital setting is significantly higher than in the government hospital ( $p = 0.029$ ).

The last known price of one vial of CCH injection was €725 in Spain, £780 in the UK and \$3,250 (actual price) and \$315 (proposed maximum price) in the US. These values were converted to Euro to enable comparison: €941 for the UK, €2392 actual price in the US and €232 proposed price in the US (as per exchange rate of 5 January 2014). The cost of CCH injections in the US is significantly higher than in Europe ( $p = 0.033$ ). The proposed price for the US would significantly reduce the difference ( $p = 0.113$ ).

Figures 1 and 2 show the cost of treating multiple affected joints with CCH injections at the different prices available, for the government hospital setting and for the private hospital setting respectively. At the prices available in the EU, the cost of using CCH injections was not significantly higher than surgery in both the government and private hospital setting when treating one ( $p = 0.112, 0.424$ ), two ( $p = 0.09, 0.169$ ) or three ( $p = 0.085, 0.118$ ) affected joints.



**Figure 1:** Cost of treating multiple affected joints in the government hospital setting at CCH prices available.



**Figure 2:** Cost of treating multiple affected joints in the private hospital setting at CCH prices available

Breakdown of costs	Government hospital		
	1 joint, 3 injections	2 joints, 6 injections	3 joints, 9 injections
Number of joints affected and number of injections needed			
Cost of injections	€231	€462	€693
Number of out-patient visits needed (at €35 each)	9	15	21
Cost of out-patient visits	€315	€525	€735
<b>Total</b>	<b>€546</b>	<b>€987</b>	<b>€1,428</b>

**Table 1:** Cost of treating one, two or three affected joints with collagenase injections at the proposed price (€77 per vial) for the Maltese market

The cost increase to treat one additional joint at the prices available in Europe does not significantly increase the hospital's expense in both the government and private hospital setting ( $p = 0.139, 0.129$ ), both when comparing two joints over one, and three joints over two. The cost to treat two additional joints results in significantly higher costs ( $p = 0.024, 0.022$ ).

The proposed price for CCH injections in Malta was calculated to be cost-effective when compared to surgery and aftercare to treat two affected fingers. With the majority of patients undergoing treatment at the government hospital, the surgical cost of €987 was taken as the maximum total cost. When taking into consideration the cost of required out-patient visits, the proposed price was €77 per vial or less (Table 1).

## DISCUSSION

When comparing the cost of open fasciectomy in the government hospital setting to the cost of the same surgery in the private hospital setting, this difference in cost was proven to be statistically significant. Reasons for this are numerous, with the most important one being that the government hospital is fully subsidised by the government. In a private hospital setting, the hospital is dependent on the income it obtains from patients using its services to stay in business, pay bills, buy and maintain new equipment and at the same time, still offer a high standard of care. Medicines are purchased at the full price, not on tender, and no expense is subsidised by government funds.

The cost of treating one, two and three affected joints with CCH at European prices in the government hospital setting compared to the cost of open fasciectomy, showed that there was no significant increase in hospital costs. However, this could be a paradox, mainly due to the large internal variance of collagenase prices. This is especially important

when one considers that treating three affected joints with collagenase costs €7,260 in Spain and €9,204 in UK, as compared to €987 for open fasciectomy using local nerve block with sedation. The fact that the results do not show a significant difference in costs could be due to the large variance in the data. If EU prices were more homogenous, statistical results could show a significant increase in costs.

In the private hospital setting, treating one, two and three affected joints also gave no significant increase in costs when compared to open fasciectomy. However, treating three affected joints with collagenase injections costs nearly three times as much as open fasciectomy. The large variance in cost could also be the reason for this result. This highlights the need to have more homogenous prices, not just between EU member states, but also with other countries.

Apart from economic considerations, using CCH injections to replace surgery could have other benefits in the Maltese healthcare system. The government hospital, falling under the responsibility of the Health Ministry and the Finance Ministry for budgetary approval, has a responsibility to make the best use out of the limited resources available.

The government is also under pressure from the public to reduce the waiting list for surgeries. An article published in The Sunday Times of Malta on 27th October 2013 listed the Orthopaedics Department as the one with the most patients waiting to be given a date for their surgery. Most of these patients are waiting for total hip or knee replacements. Taking this into consideration, if all patients needing open fasciectomy for Dupuytren's Contracture were switched over to CCH injections, an additional twenty total knee replacements could be performed every year.



## Apart from economic considerations, using *Clostridium histolyticum* injections to replace surgery could have other benefits in the Maltese healthcare system.

### CONCLUSION

Collagenase *Clostridium histolyticum* injections, at the prices last available on the market, would not be a cost-effective option for treating Dupuytren's Contracture in the government hospital. Open fasciectomy in the state hospital costs much less than in the private sector mainly due to the running costs.

In the private sector, CCH injections are more cost-effective than open fasciectomy when only one finger is affected. When multiple fingers are affected, open fasciectomy remains the least expensive option. At the prices available in Europe, using CCH injections in the private sector would always be less expensive than surgery if only one finger is affected. With open fasciectomy and aftercare costing €3,361 per patient, CCH injections would result in savings ranging from €88 (if CCH is priced €941 at per vial) up to €736 (if CCH is priced at €725 per vial). When two or more fingers are affected, the results are reversed. With the cost of treating two fingers with CCH injections amounting to a minimum of €5,100 (when CCH injections are priced at €725 per vial), injections would be more expensive than open fasciectomy by a minimum of €1,739.

With the majority of patients having one or two fingers affected, CCH injections need to be less expensive than surgery to be cost-effective, and should ideally cost €77 or less per vial, to be at an equal cost to surgery in the government hospital.

If all patients treated at the government hospital for Dupuytren's Contracture are switched to collagenase *Clostridium histolyticum* injections, the hospital would be increasing its expenses, but at the same time it would free operating theatre hours that could be used for other procedures, thus reducing patients' waiting lists.

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### Disclaimer:

During the initial stages of the study, the corresponding author was an employee of Pfizer. At the time, the marketing authorisation for collagenase injections had already been sold by Pfizer to Auxilium Pharmaceuticals.